### (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

# (19) World Intellectual Property Organization International Bureau



## 

(43) International Publication Date 15 January 2004 (15.01.2004)

#### PCT

## (10) International Publication Number WO 2004/004644 A2

(51) International Patent Classification7:

**A61K** 

MOHI, Golam [IN/US]; Avalon at Newton Highlands, 99 Needham Street, Newton, MA 02461 (US).

(21) International Application Number:

PCT/US2003/020972

(74) Agent: CLARK, Paul, T.; Clark & Elbing LLP, 101 Federal Street, Boston, MA 02110 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,

(22) International Filing Date: 3 July 2003 (03.07.2003)

English

(25) Filing Language:

\_

(26) Publication Language:

English

(30) Priority Data:

60/394,029

5 July 2002 (05.07.2002) US

60/412,402

20 September 2002 (20.09.2002) US

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US

60/394,029 (CIP)

Filed on

5 July 2002 (05.07.2002)

US

60/412,402 (CIP) 20 September 2002 (20.09.2002)

Filed on

ionated States except 1/S). RETH

(71) Applicant (for all designated States except US): BETH ISRAEL DEACONESS MEDICAL CENTER [US/US]; 330 Brookline Avenue, Boston, MA 02215 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): NEEL, Benjamin, G. [US/US]; 7 Grove Street, Wayland, MA 01778 (US). Published:

 without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMBINATION OF MTOR INHIBITOR AND A TYROSINE KINASE INHIBITOR FOR THE TREATMENT OF NEOPLASMS

(57) Abstract: The invention features methods and compositions including an mTOR inhibitor and a tyrosine kinase inhibitor for reducing the proliferation of and enhancing the apoptosis of neoplastic cells. The addition of an MEK inhibitor to this combination further enhances the effectiveness of this therapeutic method.

